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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/004,395	01/08/1998	ROBERT D. GILMORE JR.	97,429	1172

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EXAMINER
MINNIFIELD, NITA M

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/004,395	GILMORE ET AL.
	Examiner	Art Unit
	N. M. Minnifield	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-17,20-26,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17,20-26,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 4 sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).
4) ☐ Interview Summary (PTO-413) Paper No(s).
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Applicants' amendment and Appeal Brief filed June 25, 2001 are acknowledged and have been entered. Claims 19, 27 and 30 have been canceled. Claims 14-17, 20-26, 28 and 29 have been amended. Claims 14-17, 20-26, 28 and 29 are now pending in the present application. It is noted that upon further review/consideration and search prosecution has been re-opened and the following Office Action is NON-FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claims 14-17 and 19-30 under 35 U.S.C. 112, second paragraph is withdrawn in view of Applicants' amendment. The rejection of claims 14-17 and 19-30 under 35 U.S.C. 102(a), as being anticipated by Ge et al, 1997 (Infection and Immunity) (i.e. Ge II) is withdrawn in view of Applicants' arguments set forth in the Appeal Brief filed June 25, 2001.

4. Claims 14-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Ge et al, 1997 (J. Bacteriology).

The claims (products and product by process) are directed to a recombinant

forth a fusion protein and that the transformed host in the recombinant process is *E. coli*.

Ge et al (J. Bacteriology, 1997) disclose a flagellin protein, FlaA, from *B. burgdorferi* having a molecular weight of 38 kD (abstract; p. 552). A lysate of *B. burgdorferi* showed strong reactivity to a protein of 38.0 kDa, which is consistent with the expression of *flaA* in growing cells (abstract). Ge et al disclose the protein sequence of the FlaA protein as well as the DNA sequence (Figure 1) and that the *B. burgdorferi* FlaA homolog contains a typical signal sequence at its N terminus including a positively charged N-terminal domain, a central hydrophobic segment and a signal peptidase I cleavage site; after cleavage the mature protein has a molecular weight of 36 kD (p. 553). Western blot analysis of cell lysates of *B. burgdorferi* indicates that a single band of approximately 38.0 kD reacted with antiserum (figure 5; p. 555). The prior art anticipates the claimed invention.

Applicant's arguments filed June 25, 2001 have been fully considered but they are not persuasive. It is noted that this response to Applicants' arguments only addresses the arguments as they pertain to Ge I (J. Bacteriology, 1997).

Applicants have argued that Ge I does not disclose, expressly or imply, the utility of FlaA protein as a diagnostic reagent. It is noted that the claims are directed to a product comprising a FlaA protein which the prior art discloses. The claims are not directed to methods of making or methods of diagnosis. In response to applicant's argument that a diagnostic reagent is not disclosed, a recitation of the intended use of the claimed invention must result in a structural

distinguish the claimed invention from the prior art. If the prior art structure is

capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

In response to applicant's arguments, the recitation of diagnostic reagent has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

It is also noted that the recitation of "recombinant" is viewed as a process limitation.

Applicants have asserted that Ge I must be enabling and describe the claimed invention sufficiently to have placed it in the possession of a person of ordinary skill in the field of the invention; Ge I does not teach one of skill in the art how to accomplish a diagnostic assay with FlaA as a reagent or how to analyze results and data of such assay. It is noted that the claims are not directed to how to accomplish a diagnostic assay with FlaA as a reagent or how to analyze results and data of such assay. The claims are directed to a FlaA protein, which the prior art discloses. It is noted that a claim is anticipated if each element of

under principles of inherency, in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice.

5. Claims 14, 16, 20, 24 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Fikrig et al (WO 97/42325).

Fikrig et al disclose a P37 protein to be used in the diagnosis of Lyme disease (abstract; pages 7, 10, 11 and 14-15). Fikrig et al disclose the use of fusion proteins (abstract; p. 23). The prior art anticipates the claimed invention.

Applicant's arguments filed June 25, 2001 have been fully considered but they are not persuasive. Applicants have asserted that the P37 protein of Fikrig et al is not the same as the 37-kDa FlaA or P37 protein of the present invention. Applicants have asserted that the nucleic acid sequence (SEQ ID NO: 6) of Fikrig et al is not the same as the nucleic acid sequence (SEQ ID NO: 2) of the claimed invention. However, it is noted that the rejected claims (14, 16, 20, 24 and 26) do not recite DNA or amino acid sequences; only a FlaA protein, which Applicants have stated, is P37. Therefore, the prior art discloses the protein and that it is a diagnostic reagent.

6. Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Grodzicki et al (1988), Hansen et al (1988), Johnson et al (1996), or Gassmann et al (1989).

Grodzicki et al discloses a flagellar protein from *Borrelia burgdorferi* (abstract). Grodzicki et al discloses that the flagellar antigen is superior to the

Hansen et al discloses a flagellar protein from *Borrelia burgdorferi* that was used in diagnostic testing (abstract; p. 345, col. 2). Hansen et al discloses that the flagellar protein is easy to purify in sufficient quantity and is a suitable reference antigen for routine serodiagnosis of Lyme disease (abstract). Hansen et al discloses that the aim of the study was to develop a more sensitive serological assay using a single *Borrelia* antigen (p. 338, col. 1). Hansen et al discloses *B. burgdorferi* flagellum showed an early and strong immune response against the 41-kD band corresponding to flagellum (p. 338, col. 2; p. 344, col. 2). *B. burgdorferi* flagellum was purified and used as the antigen in an ELISA (p. 338, col. 2; materials and methods). The ELISA using the *B. burgdorferi* flagellum as a test antigen significantly improves serodiagnosis of Lyme disease (p. 344, col. 1). "The use of a single purified antigen such as the *B. burgdorferi* flagellum, as the test antigen eliminates the detection of such unspecific antibodies." (p. 344, col. 2).

Johnson et al discloses a purified flagellar antigen from *Borrelia burgdorferi* (abstract) and suggest its use in diagnosis of Lyme disease (p. 346).

Gassmann et al discloses a 41 kDa flagellar protein from *Borrelia burgdorferi* that "...appears to an immunodominant antigen producing an early and strong response in most if not all individuals during infections in humans. It would represent a very good antigen for serodiagnosis of Lyme disease, if its crossreactivity with flagella of other bacteria was low." (abstract). Gassmann et al discloses that the entire flagellar protein or parts of it may represent appropriate antigens for specific serodiagnosis of *Borrelia burgdorferi* infections

The recitation of diagnostic reagent has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

The recitation of "recombinant" is viewed as a process limitation.

The claim is directed to a product; the recitation (diagnostic reagent) of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

7. Claims 14, 16, 20, 24 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Fikrig et al 1997 (Immunity).

Fikrig et al discloses antigens, P37, from *Borrelia burgdorferi* for diagnosis of Lyme disease (abstract; p. 531, col. 2; p. 538). Fikrig et al discloses that P37

Fikrig et al discloses methods of making P37 by recombinant means (using

expression vectors, host cells, *E. coli*, etc) as well as making fusion proteins that comprise P37 and GT (p. 538).

8. Claims 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ge et al taken with Fikrig et al (WO 97/42325 or Immunity, 1997).

Ge et al (J. Bacteriology, 1997) teaches a flagellin protein, FlaA, from *B. burgdorferi* having a molecular weight of 38 kD (abstract; p. 552). A lysate of *B. burgdorferi* showed strong reactivity to a protein of 38.0 kDa, which is consistent with the expression of *flaA* in growing cells (abstract). Ge et al teaches the protein sequence of the FlaA protein as well as the DNA sequence (Figure 1) and that the *B. burgdorferi* FlaA homolog contains a typical signal sequence at its N terminus including a positively charged N-terminal domain, a central hydrophobic segment and a signal peptidase I cleavage site; after cleavage the mature protein has a molecular weight of 36 kD (p. 553). Western blot analysis of cell lysates of *B. burgdorferi* indicates that a single band of approximately 38.0 kD reacted with antiserum (figure 5; p. 555). The prior art teaches the claimed invention except for the process steps of making the recombinant FlaA protein.

However, Fikrig et al teaches a P37 protein from *Borrelia burgdorferi* to be used in the diagnosis of Lyme disease (abstract; pages 7, 10, 11 and 14-15). Fikrig et al teaches the use of fusion proteins (abstract; p. 23). Fikrig et al teaches making recombinant DNA molecules and transformed host cells (i.e. *E. coli*) and their protein products, fusion proteins or proteins of *Borrelia burgdorferi*

protein (pp 23-24 pp 29-32 p 79)

Fikrig et al teaches antigens, P37, from *Borrelia burgdorferi* for diagnosis of Lyme disease (abstract; p. 531, col. 2; p. 538). Fikrig et al teaches that P37 appears to be expressed in the early stages of mammalian infection (p. 534). Fikrig et al teaches methods of making P37 by recombinant means (using expression vectors, host cells, *E. coli*, etc) as well as making fusion proteins that comprise P37 and GT (p. 538).

Therefore it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the DNA of Ge et al who teaches a FlaA protein in the methods of making recombinant proteins and fusions proteins from *Borrelia burgdorferi* as set forth in Fikrig et al for the purpose of diagnosis of Lyme disease in a patient. It is noted that even though Fikrig et al teaches DNA sequences of *Borrelia burgdorferi* proteins, the reference is not relied upon for the DNA sequences. Fikrig et al teaches making *Borrelia burgdorferi* proteins recombinantly for the diagnosis of Lyme disease (WO 97/42325, pp. 8-9). It would have been obvious to a person of ordinary skill in the art to use the combination of teachings in these two prior art references with the reasonable expectation of success of making a diagnostic reagent, for early detection of Lyme disease, produced by recombinant means. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

9. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

N. M. Minnifield
Primary Examiner
Art Unit 1645

nmm

March 29, 2002